Challenges in modelling the dynamics of infectious diseases at the wildlife-human interface*

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Abstract

The Covid-19 pandemic is of zoonotic origin, and many other emerging infections of humans have their origin in an animal host population. We review the challenges involved in modelling the dynamics of wildlife-human interfaces governing infectious disease emergence and spread. We argue that we need a better understanding of the dynamic nature of such interfaces, the underpinning diversity of pathogens and host-pathogen association networks, and the scales and frequencies at which environmental conditions enable spillover and host shifting from animals to humans to occur. The major drivers of the emergence of zoonoses are anthropogenic, including the global change in climate and land use. These, and other ecological processes pose challenges that must be overcome to counterbalance pandemic risk. The development of more detailed and nuanced models will provide better tools for analysing and understanding infectious disease emergence and spread.

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Introduction

The majority of emerging infectious diseases recorded in the last century were of zoonotic origin. Their transmission from wildlife or domestic animals encompasses diverse routes of spillover, through direct contact and aerosol to vector-borne.[36] While some pathogens have been known for decades to cause recurrent spillover events (e.g. rabies virus, *Borrelia burgdorferi* and *Yersinia pestis*), new pathogens are discovered sporadically following outbreaks. For example, Hendra and Nipah viruses were identified twenty years ago, and are now recognised as members of the family Paramyxoviridae, comprising viruses infecting mammals, birds and reptiles with various levels of host specificity. The growing pace of research in this field, fuelled by the ability to combine and mine global medical, genomic, ecological and environmental datasets, has generated statistical models and risk maps of increasing complexity, either for emerging diseases as a whole[26] or for specific pathogens such as Ebola virus.[61] However, many spillover events remain unobserved or unreported,[23] and our ability to predict or prevent zoonotic spillover is in its infancy.[4]

We describe challenges that arise in modelling the dynamics of infectious disease spillover and host shifting at the interface between humans, wildlife and domestic animals. An earlier paper described eight challenges in modelling disease ecology in multi-host multi-agent systems.[10] We show that progress has been made on some, but not all of those challenges; and in the meantime new challenges have arisen. A companion paper addresses the evolution of pandemic capability in the human population.[24] We refer to spillover as the infection of novel host populations, but not necessarily novel

host species, whereas we refer to host shifting as the infection of a novel host species (including the expansion of a pathogen's host range). We define the interface as a biological system in which direct or indirect interactions between animal species and humans may result in cross-species transmission and the sharing of pathogens. The interface involves at least three species: the human host, an animal host, and the pathogen. Many more species may be involved, either directly or indirectly.

1 Mapping the interface

Historically, models for zoonotic, inter–species or vector–borne disease dynamics have assumed that the transmission rate is proportional to the local abundances of the donor and recipient species.[3] While this generally works well for pathogens with clearly identified routes of transmission, such as rabies or mosquito-borne diseases, many gaps remain in our understanding of the routes of zoonotic spillover from wildlife. Given that spillover events are generally rare or difficult to observe, it is a major challenge to quantify their probability and identify risk factors across time and space.[4]

1.1 Blind spots for models of spillover

Many spillover events are undetected, misdiagnosed or unreported. Surveillance is particularly poor in rural regions, and is generally weaker in lower income countries. We only tend to know about spillover events that result in larger outbreaks, or about localised clusters of spillover events. As a result, the routes of spillover and associated risk factors are often unknown, or have to be inferred from anecdotal evidence. When a new virus is identified in humans or domestic animals, it often takes years to determine its zoonotic origin. For example, Ebola virus was first identified in 1976 with over 25 reported outbreaks in central and Western Africa, but still lacks conclusively known routes of zoonotic spillover. The role of bats as the putative source of the West African outbreak in 2013 remains speculative.[45] There is still uncertainty about which species act as reservoirs of Ebola virus, the prevalence of infection in wildlife, and the modes of transmission within or between species. Although several risk maps for Ebola spillover in Africa have been published,[32,61] they all rely on multiple layers of statistical inference based on very sparse data and simplifying assumptions. For the time being, the main value of risk maps such as these is in identifying blind spots, that is the myriads of unknown pathogens, reservoirs and conditions

that enable pathogen transmission at wildlife-human interfaces, rather than hotspots. Epidemiologists must work closely with ecologists, virologists and social scientists to understand the available evidence on the joint distributions of wildlife, pathogens, domestic animals and humans, and quantify uncertainty at each level.

For zoonotic infections with well-characterised routes of spillover, and hence scope for reliable predictive modelling, the main challenge is in integrating statistical environmental models with mechanistic models of population and infection dynamics. Examples include Lassa virus transmitted by rodent urine in West Africa; hantavirus (also from rodents) in Europe, North and South America; Nipah virus in Malaysia and Bangladesh and Hendra virus in Australia, the latter two transmitted by pteropid bat species. For well identified wildlife hosts with predictable spatiotemporal distributions and abundance fluctuations, it is already possible to use predictive models to alert authorities and communities to a heightened seasonal risk of spillover (e.g. Hendra virus), or work with them to reduce or replace specific risky practices (e.g. palm sap collection and consumption in Bangladesh).

Despite limited direct evidence, two human activities are often cited as major risk factors for zoonotic spillover: the wildlife trade and forest cover change. The wildlife trade operates locally, between countries and between districts of large countries, and includes legal and illegal activity.[7,16] Tropical deforestation has resulted in those people actively involved in tree-cutting, or who settle in converted forest production landscapes immediately after land clearance, being at risk of exposure to novel pathogens. Deforestation is often driven by intensification of agriculture or other land use, and is thought to have enabled the emergence of HIV, and Hendra and Nipah viruses among others.[17] Attempting to quantify risk in each of these circumstances requires different but overlapping sets of information. In both cases we need a much deeper and more comprehensive knowledge of viral diversity, particularly in species that are widely used in the wildlife trade, but also in species that people or their domestic animals will likely be exposed to when clearing land and living in forests that have recently been converted for agriculture. Once these data become available and risk maps are compiled, using the information to support an epidemic model will still present a considerable challenge.

1.2 Mapping virus diversity

There has been a rapidly growing effort to initiate a global virome project that sets up a widely accessible library of genetic samples of viruses recorded across a broad array of tropical and temperate mammal and bird species. One aim is to understand which factors may facilitate the spillover of viruses from animal reservoirs to humans.The costs of this enterprise are non-trivial, although they are significantly less than the cost of another pandemic comparable to the Covid-19 outbreak. The expected benefits are debated, mainly by comparison with basic public health needs that are yet to be met in many parts of the world, but the funds for virus discovery would most likely come from a different pool. As we have seen with Covid-19, those at most risk from a lack of basic public health care are those that are most impacted by a pandemic.

There are major benefits of having a Global Virome Library:[35] first of all, understanding the full diversity of virus genetic structure would rapidly enhance the development of tests for infection and exposure. We now have the technological skills to develop vaccines directly from the RNA of a virus. Our ability to develop targeted vaccines will vary between different virus groups, and understanding the pitfalls and short-cuts available for developing vaccines for these groups will considerably speed the development of vaccines for future emerging pathogens. There are major hurdles too: virus diversity is undoubtedly much larger than host diversity, creating technical challenges to analyse and understand the complex networks of association. Moreover, understanding the diversity of host-pathogen associations at species level does not necessarily allow us to capture fine-scale spatiotemporal dynamics of virus spread in sufficient detail to predict pathogen spillover. The current quest to map and characterise the function of the bacterial microbiota in animals provides both hope and caution. In particular, there are still major gaps in our ability to map genotype to phenotype, whether in bacteria or viruses, limiting the insight we can gain from libraries of genome sequences. From an ecological perspective, there are gaps in our understanding of the factors that maintain global levels of biodiversity and abundance in different ecosystems.[30] We have only a rudimentary understanding of the role that undiscovered viral, bacterial and fungal pathogens play in determining the abundance and diversity of life on our planet.

Understanding the scale of virus diversity requires a deeper understanding of the rates at which diversity increases as host abundance changes, and as more hosts are sampled for novel viruses. Initial attempts to quantify virus diversity assume a constant number of viruses per host species. This seems at best naive. Species with large population sizes and broad geographical

distributions seem likely to harbour a much broader diversity of viral pathogens than rare host species with limited geographical ranges. Understanding the relationship between the number of hosts sampled and the number of viruses recorded is crucial here. Initial estimates for bats and macaques in southern China suggest that the half-saturation constant for virus discovery has values in the low to medium hundreds, with between 30 to 40 novel viruses located in bats and around a hundred in macaques.[6] These estimates of diversity need to be combined with estimates of host distribution and abundance for all major taxa of birds and mammals. Many of these data are available from the International Union for Conservation of Nature and major conservation NGO's. It remains a challenge to account for the actual distribution of pathogens if transmission cycles are not maintained throughout the entire ranges of host species. Simply using data from previous outbreaks of infectious diseases to produce risk maps is likely to prove misleading.[36] Most data are collected close to research stations and it is not easy to adjust sampling in a way that truly reflects risk.

Vector-borne diseases are among the best-mapped diseases, thanks to years of effort in the field and laboratories. There has been good progress in mapping the abundance of mosquitos and modelling their response to environmental variables. The programme led by Microsoft (*Premonition*[13]) aims at automating the monitoring of insect abundance and pathogen detection in the field, which would provide real-time risk maps on a par with weather maps. The problem of relating the insect abundance and prevalence data to risk, and then transmission, remains. Despite that, contact rates between blood-feeding insects and their animal hosts are much better understood than zoonotic contact rates between wildlife reservoirs and humans. Emerging coronaviruses and filoviruses have cast light on the trade and consumption of wild animals, but we still lack evidence to assess the spillover risk associated with specific practices. From a public health perspective, the consumption of under-cooked chicken meat in the UK or USA may be causing greater morbidity from enteric bacteria than the consumption of bat meat in West Africa, which is mainly sold already cooked in markets. Perhaps a greater challenge is to predict infection risk if the transmission pathways depend on the off-host environment. Exposure to urine from bats or rodents, for example, is difficult to measure and there could be large variations in the actual dose of infectious viruses linked to any particular route of spillover under different environmental conditions. Apparently, mapping virus diversity is a critical first step in predicting disease emergence, but dynamical animal-human interfaces challenge generalisations.

1.3 Modelling spillover risk at different scales

Given the gaps and uncertainties cited above, it is important to distinguish spillover risks at different scales in space and time. This is a particular issue when integrating multiple sources of data of varying quality or resolution. Thanks to progress in remote sensing, particularly satellite imagery combined with artificial intelligence for image analysis, environmental data of increasing quality, resolution and diversity are now available to scientists. As well as temperature, humidity and vegetation cover, it is now possible to map human population densities, trees and even some large animals from the sky. In contrast, populations of smaller animals that make up most zoonotic reservoirs, such as rodents, birds and bats, remain more challenging to map. These populations can be highly mobile or subject to large seasonal fluctuations. Although the combination of individual tracking (e.g. with GPS tags) and ecological niche modelling has improved our ability to predict animal distributions, the accuracy and resolution of these predictions must not be overestimated.

There is a variety of mechanisms by which transmission across the interface may occur,[60,61] for example hunting gorillas for bushmeat has been implicated in a number of Ebola outbreaks.[74] Cultural and social factors can lead to large variations in the risk of exposure to bat species carrying zoonotic viruses: a bat roost in a sacred grove may be off-limits, another rural roost may be regularly harvested for meat by a group of hunters, and a third urban roost may be safe from hunters while exposing thousands of passers-by to urine and faeces. Some communities actively disrupt bat roosts to chase them away, while others attract bats to collect guano. Local evidence, particularly regarding human behaviour, is essential to properly assess spillover risks. Spillover events are often contingent on factors that are localised in time and space, and the individuals and animals responsible for a particular event may be outliers in their location or behaviour. Hence there is debate about the practicability and capacity to forecast disease outbreaks and spillover events.[31,68] Successful forecasting will require an iterative approach to probabilistic prediction and testing, updating these predictions as new data become available. The difficulty of recording pathogen spillover and the complexity of the involved interactions and environmental conditions that may amplify pathogen spread require further research. The question is whether shortfalls in forecasting over meaningful time horizons stem from insufficient data or the unpredictable nature of highly dynamic human-animal interfaces. For example, a single rabid raccoon trapped in a bin in Ohio and transported to a landfill site dozens of miles away can trigger a wave front of rabies in a new location.[48] Even with a reliable

mechanistic model, forecasting the spatial spread of rabies across a state would be subject to a large stochastic variance.

1.4 Estimating the frequency of spillover

As spillover events are rarely observed, we must rely on indirect methods to infer their frequency with the help of epidemiological models. A data set collated over the last 100 years shows that approximately two new viral pathogens are reported from humans every year.[86] This followed an initial lower rate of discovery prior to 1940 when biological understanding of viruses was at a more rudimentary level. Crossovers that lead to a significant outbreak occur less frequently, but roughly 10% of those that do crossover lead to a local outbreak.[16,43]

Serological surveys are commonly used to measure population-level exposure to pathogens. For example, surveillance in China revealed that approximately 3% of people, all of whom had high previous exposure to potential reservoir bat hosts but no apparent exposure to the previously circulating SARS coronavirus, had been exposed to other similar viruses.[77] Describing these processes will require not only epidemiological models, but within-host models of competing infections incorporating cross-immunity.

When clusters of clinical cases or seropositive samples are detected, the next step is to determine whether they stemmed from a single spillover event followed by person-to-person transmission, or from multiple spillover events. This is important to assess the relative risks of onward transmission in the population or future zoonotic risk. For example, Lassa virus in West Africa, Nipah virus in Bangladesh and Puumala virus in Finland have caused numbers of sporadic outbreaks with no or little human-to-human transmission. But, as we know from avian influenza in particular, we should always be on the lookout for epidemic potential, especially as viruses mutate. Even when rare, human-to-human transmission has the potential to spiral out of control, as further discussed in this volume.[24] In the case of Lassa fever, epidemic models have shown that a small proportion of hospital cases could be attributed to human-to-human transmission, with the large variance raising the concern of superspreading events.[44] Finally, when pathogen sequences can be obtained from patients, the amount of genetic diversity within a cluster of cases can help determine common sources of transmission.

2 Modelling the impact of anthropogenic environmental changes on spillover

The threat of emerging diseases is closely linked to two unfolding anthropogenic environmental crises: climate and land use change. While attributing spillover events to the consequences of environmental changes is often speculative, it is vital to develop the capacity to predict the impact of anthropogenic changes on future spillover risk.

2.1 Climate change

Many challenges arise when modelling the effect of changes in ecosystems, and anticipating what these changes may be presents its own set of challenges. The long term global change in climate is projected to cause shifts in host and vector ranges.[33] Predicting changes in the geographical distribution of host species will require models linking habitat conditions to population dynamics and biological interactions. This is especially true for vector-borne diseases, where it is anticipated that mosquitos may move into new geographical regions, increasing the distribution of infections due to dengue and Zika viruses.[39,52] In addition, the life cycles of vectors and hosts may be modified.[51] Changes in rainfall may alter crop conditions and the population cycles of herbivores such as rodents. The thermal mismatch effect determines that hosts from cool and warm climates experience increased disease risk at abnormally warm and cool temperatures, respectively.[12,65] The challenge is to utilise these data to model the transmission of zoonoses from animal reservoirs to humans, and to determine how this risk of transmission may be changing.

2.2 Land use change

Changes in land use lead to changes in host ranges, and may increase the rate of contact between non-host species, hosts, vectors, domestic animals and humans. In other words, a complete reorganisation of the ecosystem balance. A recent study has examined how zoonotic host diversity increases in human dominated ecosystems.[18] Deforestation has been implicated in increased interactions between humans and wildlife, facilitating the transmission of zoonotic infections.[19,22,82] For example, forest fragmentation has been implicated in the transmission of Ebola[67] and malaria.[8] Increased urbanisation also leads to a potential habitat overlap of hosts and vectors from rural and urban areas, with the potential for extended life-cycles and

the expansion of the host range of pathogens. Forest conversion, especially associated with oil palm production, has been associated with outbreaks of vector-borne and zoonotic diseases.[50] Modelling these changes will be necessary to understand the drivers of zoonotic transmission. A robust model has shown that if transmission scales with the boundary between original forest habitat and the modified land that forms an agricultural matrix, then transmission rates will peak at intermediate levels of transformation.[19] Obviously the fractal nature of the boundary can only increase the magnitude of this maximum. More subtly, a stochastic realisation of the model suggests that the size of the resultant epidemic in the host population that resides in the matrix will be determined by a bifurcation that occurs at around 50% levels of conversion, both small and very large epidemics have equal chance of occurring by the time $70 - 80\%$ of the habitat is converted. The rates of transmission between the pristine habitat and the emerging agricultural matrix are always at a minimum of zero when either none or all of the habitat is converted. The importance of taking spatial scales into account has been demonstrated by the derivation of an invasion threshold using percolation theory.[15] The model, in this case for the transmission of plague (*Yersinia pestis*) in great gerbils (*Rhombomys opimus*) combined the scales of flea movements, the host's habitat, and the surveillance region. The methodology could be used to model other examples of infection transmission in fragmented landscapes.

2.3 Ecological invasions

The transport of exotic animals as domestic pets or novel livestock has the potential to spread zoonotic pathogens to new regions.[33] While this transport is deliberate on the part of humans, host animals and vectors may *hitch a ride* with cargo or in ships or aircraft, for example the accidental spread of invasive mosquitos along major transport channels.[46,69] The magnitude of these transport events are most likely dwarfed by the substantial national and international trade in wildlife species. Risk assessment models that take advantage of large-scale monitoring data are necessary to protect geographical regions from unwanted incursions.[57,59] Other deliberate movements of wildlife result from reintroductions and re-wilding. For example, the recovery of predatory pine martens (*Martes martes*) in Scotland has changed the dynamics of disease-mediated competition between two different squirrel species.[64,71] The reintroduction of wolves (*Canis lupus*) in some areas of Spain has resulted in a decrease in tuberculosis infections in wild boar (*Sus scrofa*). Model results and field

studies suggest that the effects of increased predation on the boar population is compensated for by the reduction in disease induced mortality.[76] These, and many other examples, show that non-host species may influence the dynamics of host species and pathogen transmission among those hosts. If we are to anticipate the threat to humans from potential zoonoses, we need to model the dynamics of the ecosystem as a whole.[27]

3 Modelling spillover as an ecological process

Predicting the emergence of infectious diseases at the human-animal interface requires an understanding of how a pathogen may shift from an animal reservoir to humans and emerge causing a zoonotic disease. Generally, host shifting requires a pathogen to be exposed to new hosts that exhibit a level of physiological and/or behavioural overlap with previous hosts through ecological fitting (species association such that an ecological trait profile enables infection by a pathogen without genetic change),[1,75,78,85] or the rapid adaptation of a pathogen to a new host environment in order to break potential barriers caused by variations in host competence or immunity.[58] Understanding the associations between reservoir host species, pathogens and humans can only be a critical first step in predicting emergence. This is because host species exhibit considerable variation in competence for maintaining pathogen transmission cycles[5,37,63,84] and epidemiological dynamics.[43] Host resistance resulting from past exposure may further suppress pathogen spread.[41]

3.1 Community ecology

The determination of which host species are reservoirs of infection requires an ecosystem model dissecting the contributions of all species: host, non-host and pathogen; to transmission.[21,27,38] Removing a particular species identified as a reservoir from the ecosystem will not necessarily remove the pathogen, a careful definition of what constitutes a reservoir must be combined with a model of the ecosystem interactions.[63] Pathogens should be viewed as integral components of ecosystems; it is likely that between 50% and 90% of species in natural ecosystems are parasites and pathogens of the more easily observed community species. For example, a detailed analysis of salt-marshes in California suggest that the biomass of pathogens may easily equal or exceed that of birds,[40] and the dynamics and abundance of these species is determined by the same scaling laws that determine the abundance

of free-living species. Their dynamics not only change with ecosystem composition, but can also affect that composition. A frequently cited paradigm is the dilution effect, the idea that increased biodiversity leads to decreased transmission of infection.[62,82] The corollary is that reduced biodiversity increases the risk of emergence of infection, but modelling has shown that this is not universal.[62] Models for ecosystem dynamics need to take the dynamics of pathogens into account, but a further step is required at the human interface. Only a small proportion of viruses are implicated in disease emergence.[20,83] For example, bats are frequently cited as reservoirs of infection for a number of viruses.[9,29,34] However, the fact that they are infected does not necessarily mean that they can transmit that infection.[5] There is clearly a complex interaction between life history traits of the host, the dynamics of host immunity and the zoonotic risk presented by the pathogen.[2] Models of emerging infections must take into account the ecosystem dynamics, increased contact with humans, and the transmissibility of the pathogens of interest to humans. Allometrically scaling the dynamics and abundance of species in the community may be the way forward to reduce the inherent computational complexity of these problems.

3.2 Tipping points of transmission at the human–wildlife interface.

While an epidemiological steady state may be characterised as stable, this does not exclude the possibility that an external perturbation will lead to a temporary move away from equilibrium, followed by a slow return. The term reactivity has been used to describe a measure of the instantaneous growth rate of a perturbation.[56] It is to be expected that as a steady state approaches instability then reactivity would increase, possibly resulting in a series of minor outbreaks. This could be the case where an ecosystem with pathogens is about to experience a spillover to a new host species, for example as the human interface is approached. Another proposed measure is the maximum possible response to perturbation, or the size of the amplification envelope.[56] While these measures have been demonstrated in simple epidemic models, it is unclear if the signatures that are generated would be observed in ecosystems. Recently the theory of stochastic processes has been used to model early warning signals for a population approaching a tipping point.[11,47,73] It remains a challenge to reconcile the signatures that can be derived from models with signatures that may be observable in the field.[28] Achieving this at the environment-human interface would provide an early warning signal that a zoonotic infection could *cross species* to humans.

3.3 Modelling the wildlife-livestock-human interface

Domesticated (livestock and companion) animals share a numbers of parasite species with wildlife and are an important source of zoonotic spillover.[54,66,79] There is a pressing need to understand what brings about the spread of a pathogen from wildlife to livestock and human populations, and hence to predict which other pathogens, hitherto not identified, might be next to emerge along such transmission routes.[49] Well-known examples to date are avian influenza H5N1, transmitted from wild birds through farmed poultry to humans, and bovine tuberculosis transmitted from a variety of wildlife reservoirs through cattle to humans.[81] Cross-species transmission of viruses from fruit bats via pigs (Nipah virus), horses (Hendra virus) and camels (MERS) has also been recorded.[42] Bat species are also suspected (but not yet confirmed) reservoir species of the novel coronavirus (SARS-CoV-2), that has spilled over from humans into farmed minks, with subsequent infection of farm workers from minks.[55] Currently, databases of host-parasite interactions compiled from primary research articles or published molecular sequences provide the most compelling evidence of the role of domestic species in pathogen spread at the human-animal interface,[70,80] although such approaches provide only a static snapshot. More recently, comparative and structural analysis of pathogen-binding receptor molecules have aided in the identification of the potential hosts for cross-species transmission of viruses such as SARS-CoV2.[14] Dynamic models linking pathogen prevalence in wildlife, animal production and health risk are required.

Arguably, the intensity of animal production, farming and pet keeping practices are key features that distinguish pathogen spillover along domestic versus sylvatic transmission routes. Farming practices that may impact pathogen spread and the emergence of infectious disease include the release of antibiotics.[53,66] Developing models that can be used to mitigate the spread of antibiotic resistance presents another challenge. Future models may also explore the epidemiological and host-pathogen co-evolutionary dynamics arising from animal domestication, given that pathogen adaptation to domestic transmission cycles may result in lineage selection for optimised persistence. For example, lineage selection for intermediate virulence appears to be the case for the generalist protozoan *Toxoplasma gondii* within its domestic transmission cycle, since the wide distribution of domestic cats and house mice facilitates a balance between lower host mortality and the ability to superinfect mice previously infected with a less virulent lineage.[72] Whether pathogens specifically adapt to features of domestic species such as high abundance and individual clustering compared to wildlife host equivalents, and whether such specific adaptions may facilitate spillover to

humans and other animals, may be promising avenues for future research.

Conclusion

We have reviewed the challenges involved in modelling the dynamics of infectious diseases at the wildlife-human interface. We have argued that the precise nature of the interface is not well known, as it is rarely detected and never observed directly. We need more information on the diversity of pathogens at the interface, especially viruses, and the scales and frequencies at which they transmit. This can only be achieved through increased data collection and surveillance. The major drivers of the emergence of zoonoses are anthropogenic. These include the global change in climate modifying the ranges of hosts and pathogens, as well as changes in land use increasing contact rates between human and animal hosts. Models will have a significant role to play in predicting the impact of these changes on disease dynamics. Ecological processes can move pathogen transmission towards tipping points, facilitating transmission. Eco-epidemiological models are required to understand the transmission of infections between host species in an ecosystem, the influence of the wider ecosystem species on host and pathogen dynamics, and to suggest the potential for spillover events to occur. In some cases domestic animals may act as an intermediate host, in the sense that they contact infected wild animals and have close contact with humans. Modelling infection dynamics in domestic animals requires a different representation of host population dynamics and contact structures than that of wild animal populations. Once a pathogen has infected a human host, it is not necessarily the case that a zoonotic disease will establish in the population. Apparently, pathogen spillover and host shifting are governed by complex and dynamic interactions among animal and human hosts at different organisational levels, challenging modellers to deal with sources of uncertainty and finding generalisations for robust predictions.

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